

WHAT IS CLAIMED IS:

1. An isolated protein complex comprising two proteins, the protein complex selected from the group consisting of:

- 5 (i) a complex of a first protein and a second protein;
- (ii) a complex of a fragment of said first protein and said second protein;
- (iii) a complex of said first protein and a fragment of said second protein; and
- (iv) a complex of a fragment of said first protein and a fragment of said second protein, wherein said first and second proteins are selected from the group consisting of:

- 10 (a) said first protein is ER-alpha and said second protein is PN12364; and
- (b) said first protein is ER-beta and said second protein is PN12365.

2. The protein complex of claim 1, wherein said protein complex comprises said first protein and said second protein.

3. The protein complex of claim 1, wherein said protein complex comprises a fragment of said first protein and said second protein or said first protein and a fragment of said second protein.

4. The protein complex of claim 1, wherein said protein complex comprises fragments of said first protein and said second protein.

5. An isolated antibody selectively immunoreactive with a protein complex of claim 1.

6. The antibody of claim 5, wherein said antibody is a monoclonal antibody.

7. A method for diagnosing a physiological disorder in an animal, which comprises assaying for:

- (a) whether a protein complex set forth in claim 1 is present in a tissue extract;
- (b) the ability of proteins to form a protein complex set forth in claim 1; and
- (c) a mutation in a gene encoding a protein of a protein complex set forth in claim

8. The method of claim 7, wherein said animal is a human.
9. The method of claim 8, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.
10. The method of claim 7, wherein the diagnosis is for a predisposition to said physiological disorder.
11. The method of claim 7, wherein the diagnosis is for the existence of said physiological disorder.
12. The method of claim 7, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.
13. The method of claim 7, wherein said assay comprises a yeast two-hybrid assay.
14. The method of claim 7, wherein said assay comprises measuring *in vitro* a complex formed by combining the proteins of the protein complex, said proteins isolated from said animal.
15. The method of claim 14, wherein said complex is measured by binding with an antibody specific for said complex.
16. The method of claim 7, wherein said assay comprises mixing an antibody specific for said protein complex with a tissue extract from said animal and measuring the binding of said antibody.
17. A method for determining whether a mutation in a gene encoding one of the proteins of a protein complex set forth in claim 1 is useful for diagnosing a physiological disorder, which comprises assaying for the ability of said protein with said mutation to form a complex with the other protein of said protein complex, wherein an inability to form said complex is indicative of said mutation being useful for diagnosing a physiological disorder.

18. The method of claim 17, wherein said gene is an animal gene.
19. The method of claim 18, wherein said animal is a human.
- 5 20. The method of claim 19, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.
- 10 21. The method of claim 17, wherein the diagnosis is for a predisposition to a physiological disorder.
22. The method of claim 17, wherein the diagnosis is for the existence of a physiological disorder.
- 15 23. The method of claim 17, wherein said assay comprises a yeast two-hybrid assay.
24. The method of claim 17, wherein said assay comprises measuring *in vitro* a complex formed by combining the proteins of the protein complex, said proteins isolated from an animal.
- 20 25. The method of claim 24, wherein said animal is a human.
26. The method of claim 24, wherein said complex is measured by binding with an antibody specific for said complex.
- 25 27. A non-human animal model for a physiological disorder wherein the genome of said animal or an ancestor thereof has been modified such that the formation of a protein complex set forth in claim 1 has been altered.
- 30 28. The non-human animal model of claim 27, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

29. The non-human animal model of claim 27, wherein the formation of said protein complex has been altered as a result of:

(a) over-expression of at least one of the proteins of said protein complex;

(b) replacement of a gene for at least one of the proteins of said protein complex with a gene from a second animal and expression of said protein;

(c) expression of a mutant form of at least one of the proteins of said protein complex;

(d) a lack of expression of at least one of the proteins of said protein complex; or

(e) reduced expression of at least one of the proteins of said protein complex.

30. A cell line obtained from the animal model of claim 27.

31. A non-human animal model for a physiological disorder, wherein the biological activity of a protein complex set forth in claim 1 has been altered.

32. The non-human animal model of claim 31, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

33. The non-human animal model of claim 31, wherein said biological activity has been altered as a result of:

(a) disrupting the formation of said complex; or

(b) disrupting the action of said complex.

34. The non-human animal model of claim 31, wherein the formation of said complex is disrupted by binding an antibody to at least one of the proteins which form said protein complex.

35. The non-human animal model of claim 31, wherein the action of said complex is disrupted by binding an antibody to said complex.

36. The non-human animal model of claim 31, wherein the formation of said complex is disrupted by binding a small molecule to at least one of the proteins which form said protein complex.

5 37. The non-human animal model of claim 31, wherein the action of said complex is disrupted by binding a small molecule to said complex.

38. A cell in which the genome of cells of said cell line has been modified to produce at least one protein complex set forth in claim 1.

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39. A cell line in which the genome of the cells of said cell line has been modified to eliminate at least one protein of a protein complex set forth in claim 1.

40. A composition comprising:

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a first expression vector having a nucleic acid encoding a first protein or a homologue or derivative or fragment thereof; and

a second expression vector having a nucleic acid encoding a second protein, or a homologue or derivative or fragment thereof, wherein said first and said second proteins are the proteins of claim 1.

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41. A host cell comprising:

a first expression vector having a nucleic acid encoding a first protein which is first protein or a homologue or derivative or fragment thereof; and

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a second expression vector having a nucleic acid encoding a second protein which is second protein, or a homologue or derivative or fragment thereof thereof, wherein said first and said second proteins are the proteins of claim 1.

42. The host cell of claim 41, wherein said host cell is a yeast cell.

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43. The host cell of claim 41, wherein said first and second proteins are expressed in fusion proteins.

44. The host cell of claim 41, wherein one of said first and second nucleic acids is linked to a nucleic acid encoding a DNA binding domain, and the other of said first and second nucleic acids is linked to a nucleic acid encoding a transcription-activation domain, whereby two fusion proteins can be produced in said host cell.

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45. The host cell of claim 41, further comprising a reporter gene, wherein the expression of the reporter gene is determined by the interaction between the first protein and the second protein.

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46. A method for screening for drug candidates capable of modulating the interaction of the proteins of a protein complex, the protein complex selected from the group consisting of the protein complexes of claim 1, said method comprising

(i) combining the proteins of said protein complex in the presence of a drug to form a first complex;

(ii) combining the proteins in the absence of said drug to form a second complex;

(iii) measuring the amount of said first complex and said second complex; and

(iv) comparing the amount of said first complex with the amount of said second complex,

wherein if the amount of said first complex is greater than, or less than the amount of said second complex, then the drug is a drug candidate for modulating the interaction of the proteins of said protein complex.

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47. The method of claim 46, wherein said screening is an *in vitro* screening.

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48. The method of claim 46, wherein said complex is measured by binding with an antibody specific for said protein complexes.

49. The method of claim 46, wherein if the amount of said first complex is greater than the amount of said second complex, then said drug is a drug candidate for promoting the interaction of said proteins.

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50. The method of claim 46, wherein if the amount of said first complex is less than the amount of said second complex, then said drug is a drug candidate for inhibiting the interaction of said proteins.

5 51. A drug useful for treating a physiological disorder identified by the method of claim 46.

52. The drug of claim 51, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

10 53. A method of screening for drug candidates useful in treating a physiological disorder which comprises the steps of:

(a) measuring the activity of a protein selected from the group consisting of a first protein and a second protein in the presence of a drug, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1,

15 (b) measuring the activity of said protein in the absence of said drug, and

(c) comparing the activity measured in steps (1) and (2),

wherein if there is a difference in activity, then said drug is a drug candidate for treating said physiological disorder.

20 54. A drug useful for treating a physiological disorder identified by the method of claim 53.

55. The drug of claim 54, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

25 56. A method for selecting modulators of a protein complex formed between a first protein or a homologue or derivative or fragment thereof and a second protein or a homologue or derivative or fragment thereof, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

providing the protein complex;

30 contacting said protein complex with a test compound; and

determining the presence or absence of binding of said test compound to said protein complex.

57. A modulator useful for treating a physiological disorder identified by the method of claim 56.

5 58. The modulator of claim 57, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

59. A method for selecting modulators of an interaction between a first protein and a second protein, said first protein or a homologue or derivative or fragment thereof and said second protein or a homologue or derivative or fragment thereof, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

10 contacting said first protein with said second protein in the presence of a test compound; and

15 determining the interaction between said first protein and said second protein.

60. The method of claim 59, wherein at least one of said first and second proteins is a fusion protein having a detectable tag.

20 61. The method of claim 59, wherein said step of determining the interaction between said first protein and said second protein is conducted in a substantially cell free environment.

62. The method of claim 59, wherein the interaction between said first protein and said second protein is determined in a host cell.

25 63. The method of claim 62, wherein said host cell is a yeast cell.

64. The method of claim 59, wherein said test compound is provided in a phage display library.

30 65. The method of claim 59, wherein said test compound is provided in a combinatorial library.



66. A modulator useful for treating a physiological disorder identified by the method of claim 59.

67. The modulator of claim 66, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

68. A method for selecting modulators of a protein complex formed from a first protein or a homologue or derivative or fragment thereof, and a second protein or a homologue or derivative or fragment thereof, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

contacting said protein complex with a test compound; and

determining the interaction between said first protein and said second protein.

69. A modulator useful for treating a physiological disorder identified by the method of claim 68.

70. The modulator of claim 69, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

71. A method for selecting modulators of an interaction between a first polypeptide and a second polypeptide, said first polypeptide being a first protein or a homologue or derivative or fragment thereof and said second polypeptide being a second protein or a homologue or derivative or fragment thereof, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

providing in a host cell a first fusion protein having said first polypeptide, and a second fusion protein having said second polypeptide, wherein a DNA binding domain is fused to one of said first and second polypeptides while a transcription-activating domain is fused to the other of said first and second polypeptides;

providing in said host cell a reporter gene, wherein the transcription of the reporter gene is determined by the interaction between the first polypeptide and the second polypeptide;

allowing said first and second fusion proteins to interact with each other within said host cell in the presence of a test compound; and

determining the presence or absence of expression of said reporter gene.

5 72. The method of claim 71, wherein said host cell is a yeast cell.

73. A modulator useful for treating a physiological disorder identified by the method of claim 71.

10 74. The modulator of claim 73, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

75. A method for identifying a compound that binds to a protein in vitro, wherein said protein is selected from the group consisting of the proteins of claim 1, said method comprising:

15 contacting a test compound with said protein for a time sufficient to form a complex and

detecting for the formation of a complex by detecting said protein or the compound in the complex,

so that if a complex is detected, a compound that binds to protein is identified.

20 76. A compound useful for treating a physiological disorder identified by the method of claim 75.

25 77. The compound of claim 76, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

30 78. A method for selecting modulators of an interaction between a first polypeptide and a second polypeptide, said first polypeptide being a first protein or a homologue or derivative or fragment thereof and said second polypeptide being a second protein or a homologue or derivative or fragment thereof, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

providing atomic coordinates defining a three-dimensional structure of a protein complex formed by said first polypeptide and said second polypeptide; and

designing or selecting compounds capable of modulating the interaction between a first polypeptide and a second polypeptide based on said atomic coordinates.

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79. A modulator useful for treating a physiological disorder identified by the method of claim 78.

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80. The modulator of claim 79, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

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81. A method for providing inhibitors of an interaction between a first polypeptide and a second polypeptide, said first polypeptide being a first protein or a homologue or derivative or fragment thereof and said second polypeptide being a second protein or a homologue or derivative or fragment thereof, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

providing atomic coordinates defining a three-dimensional structure of a protein complex formed by said first polypeptide and said second polypeptide; and

designing or selecting compounds capable of interfering with the interaction between a first polypeptide and a second polypeptide based on said atomic coordinates.

82. An inhibitor useful for treating a physiological disorder identified by the method of claim 81.

25 83. The inhibitor of claim 82, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

84. A method for selecting modulators of a protein, wherein said protein is selected from the group consisting of the proteins of claim 1, said method comprising:

30 contacting said protein with a test compound; and  
determining binding of said test compound to said protein.

85. The method of claim 84, wherein said test compound is provided in a phage display library.

86. The method of claim 84, wherein said test compound is provided in a combinatorial library.

5 87. A modulator useful for treating a physiological disorder identified by the method of claim 84.

88. The modulator of claim 87, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

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89. A method for modulating, in a cell, a protein complex having a first protein interacting with a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

administering to said cell a compound capable of modulating said protein complex.

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90. The method of claim 89, wherein said compound is selected from the group consisting of:

(a) a compound which is capable of interfering with the interaction between said first protein and said second protein,

(b) a compound which is capable of binding at least one of said first protein and said second protein,

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(c) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of said second protein and capable of binding said first protein,

(d) a compound which comprises a peptide capable of binding said first protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of said second protein of the same length,

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(e) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of said first protein and capable of binding said second protein,

(f) a compound which comprises a peptide capable of binding said second protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of said first protein of the same length,

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(g) a compound which is an antibody immunoreactive with said first protein or said second protein,

(h) a compound which is a nucleic acid encoding an antibody immunoreactive with said first protein or said second protein,

(i) a compound which modulates the expression of said first protein or said second protein,

(j) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding said first protein or complement thereof, and

(k) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding said second protein or complement thereof.

91. A method for modulating, in a cell, a protein complex having a first protein interacting with a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

administering to said cell a peptide capable of interfering with the interaction between said first protein and said second protein, wherein said peptide is associated with a transporter capable of increasing cellular uptake of said peptide.

92. The method of claim 91, wherein said peptide is covalently linked to said transporter which is selected from the group consisting of penetratins, *l*-Tat<sub>49-57</sub>, *d*-Tat<sub>49-57</sub>, retro-inverso isomers of *l*- or *d*-Tat<sub>49-57</sub>, L-arginine oligomers, D-arginine oligomers, L-lysine oligomers, D-lysine oligomers, L-histidine oligomers, D-histidine oligomers, L-ornithine oligomers, D-ornithine oligomers, short peptide sequences derived from fibroblast growth factor, Galparan, and HSV-1 structural protein VP22, and peptoid analogs thereof.

93. A method for modulating, in a cell, the interaction of a protein with a ligand, wherein said protein is selected from the group consisting of the first or second proteins of claim 1, said method comprising:

administering to said cell a compound capable of modulating said interaction.

94. The method of claim 93, wherein said protein is one of said first or second proteins and said ligand is the other of said first or second proteins

95. The method of claim 93, wherein said compound is selected from the group consisting of:

- (a) a compound which interferes with said interaction,
- (b) a compound which binds to said protein or said ligand,
- (c) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of said protein and capable of binding said ligand,

(d) a compound which comprises a peptide capable of binding said ligand and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of said protein of the same length,

(e) a compound which is an antibody immunoreactive with said protein or said ligand,

(f) a compound which is a nucleic acid encoding an antibody immunoreactive with said ligand or said protein,

(g) a compound which modulates the expression of said protein or said ligand, and

(h) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding said ligand or said protein or complement thereof.

96. A method for modulating neuronal death in a patient having a physiological disorder comprising:

modulating a protein complex having a first protein interacting with a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1.

97. The method of claim 96, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

98. A method for modulating neuronal death in a patient having physiological disorder comprising:

administering to the patient a compound capable of modulating a protein complex having a first protein interacting with a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1.

99. The method of claim 98, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

100. The method of claim 98, wherein said compound is selected from the group consisting of:

(a) a compound which is capable of interfering with the interaction between said first protein and said second protein,

(b) a compound which is capable of binding at least one of said first protein and said second protein,

(c) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of a second protein and capable of binding a first protein,

(d) a compound which comprises a peptide capable of binding a first protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of a second protein of the same length,

(e) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of first protein and capable of binding a second protein,

(f) a compound which comprises a peptide capable of binding a second protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of a first protein of the same length,

(g) a compound which is an antibody immunoreactive with a first protein or a second protein,

(h) a compound which is a nucleic acid encoding an antibody immunoreactive with a first protein or a second protein,

(i) a compound which modulates the expression of a first protein or a second protein,

(j) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding a first protein or complement thereof, and

(k) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding a second protein or complement thereof

101. A method for modulating neuronal death in a patient having physiological disorder comprising:

administering to said cell a peptide capable of interfering with the interaction between a first protein and a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, wherein said peptide is associated with a transporter capable of increasing cellular uptake of said peptide.

102. The method of claim 101, wherein said peptide is covalently linked to said transporter which is selected from the group consisting of penetratins, *l*-Tat<sub>49-57</sub>, *d*-Tat<sub>49-57</sub>, retro-inverso isomers of *l*- or *d*-Tat<sub>49-57</sub>, L-arginine oligomers, D- arginine oligomers, L-lysine oligomers, D-lysine oligomers, L-histidine oligomers, D-histidine oligomers, L-ornithine oligomers, D-ornithine oligomers, short peptide sequences derived from fibroblast growth factor, Galparan, and HSV-1 structural protein VP22, and peptoid analogs thereof.
103. A method for treating a physiological disorder comprising:  
administering to a patient in need of treatment a compound capable of modulating a protein complex having a first protein interacting with a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1.
104. The method of claim 103, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.
105. The method of claim 103, wherein said compound is selected from the group consisting of:  
(a) a compound which is capable of interfering with the interaction between said first protein and said second protein,  
(b) a compound which is capable of binding at least one of said first protein and said second protein,  
(c) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of said second protein and capable of binding said first protein,  
(d) a compound which comprises a peptide capable of binding said first protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of said second protein of the same length,  
(e) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of first protein and capable of binding said second protein,  
(f) a compound which comprises a peptide capable of binding said second protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of said first protein of the same length,



(g) a compound which is an antibody immunoreactive with said first protein or said second protein,

(h) a compound which is a nucleic acid encoding an antibody immunoreactive with said first protein or said second protein,

(i) a compound which modulates the expression of said first protein or said second protein,

(j) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding a first protein or complement thereof,

(k) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding a second protein or complement thereof, and

(l) a compound which is capable of strengthening the interaction between said first protein and said second protein.

106. A method for treating a physiological disorder comprising:

administering to said cell a peptide capable of interfering with the interaction between a first protein and a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, wherein said peptide is associated with a transporter capable of increasing cellular uptake of said peptide.

107. The method of claim 106, wherein said peptide is covalently linked to said transporter which is selected from the group consisting of penetratins, *l*-Tat<sub>49-57</sub>, *d*-Tat<sub>49-57</sub>, retro-inverso isomers of *l*- or *d*-Tat<sub>49-57</sub>, L-arginine oligomers, D-arginine oligomers, L-lysine oligomers, D-lysine oligomers, L-histidine oligomers, D-histidine oligomers, L-ornithine oligomers, D-ornithine oligomers, short peptide sequences derived from fibroblast growth factor, Galparan, and HSV-1 structural protein VP22, and peptoid analogs thereof.

108. The method of claim 106, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

109. A method for treating a physiological disorder comprising:

administering to a patient in need of treatment a compound capable of modulating the activity of a first protein or a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1.

5 110. The method of claim 109, wherein said physiological disorder is selected from the group consisting of breast cancer and pituitary adenomas.

111. The method of claim 109, wherein the activity is the interaction of said first protein or said second protein with a ligand.

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112. The method of claim 111, wherein said ligand is the other of said first or second protein.

113. A method of modulating activity in a cell of a protein, said protein being first protein or a second protein selected from the group consisting of the proteins of claim 1, said method comprising:

administering to said cell a compound capable of modulating said protein.

114. The method of claim 113, wherein said compound is selected from the group consisting of:

(a) a compound which is capable of binding said protein,

(b) a compound which comprises a peptide having a contiguous span of at least 4 amino acids of a first protein and capable of binding a second protein,

(c) a compound which comprises a peptide capable of binding a second protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of a first protein of the same length,

(d) a compound which is an antibody immunoreactive with said protein,

(e) a compound which is a nucleic acid encoding an antibody immunoreactive with said protein, and

(f) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding said protein or complement thereof.

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115. A method for modulating activities of a protein in a cell, said protein being a first protein or a second protein selected from the group consisting of the proteins of claim 1, said method comprising:

administering to said cell a peptide having a contiguous span of at least 4 amino acids of one of said first or second proteins and capable of binding the other of said first or second proteins, wherein said peptide is associated with a transporter capable of increasing cellular uptake of said peptide.

116. The method of claim 115, wherein said peptide is covalently linked to said transporter which is selected from the group consisting of penetratins, *l*-Tat<sub>49-57</sub>, *d*-Tat<sub>49-57</sub>, retro-inverso isomers of *l*- or *d*-Tat<sub>49-57</sub>, L-arginine oligomers, D-arginine oligomers, L-lysine oligomers, D-lysine oligomers, L-histidine oligomers, D-histidine oligomers, L-ornithine oligomers, D-ornithine oligomers, short peptide sequences derived from fibroblast growth factor, Galparan, and HSV-1 structural protein VP22, and peptoid analogs thereof.

117. An isolated nucleic acid encoding a protein selected from the group consisting of a protein comprising an amino acid sequence set forth in SEQ ID NO:4 and a protein comprising an amino acid sequence set forth in SEQ ID NO:6.

118. The isolated nucleic acid sequence of claim 117 which is selected from the group consisting of a nucleic acid comprising nucleotides 1-528 of SEQ ID NO:3 or complement thereof and a nucleic acid comprising nucleotides 1-654 of SEQ ID NO:5.

119. An isolated nucleic acid encoding a protein selected from the group consisting of (a) a protein comprising an amino acid sequence which is at least 70% identical to the amino acid sequence set forth in SEQ ID NO:4 and which is capable of interacting with ER-alpha and (b) a protein comprising an amino acid sequence which is at least 70% identical to the amino acid sequence set forth in SEQ ID NO:6 and which is capable of interacting with ER-beta.

120. The isolated nucleic acid of claim 119, wherein said protein is ligand is ER-alpha.

121. The isolated nucleic acid of claim 119, wherein said ligand is ER-beta.

122. An isolated nucleic acid comprising a nucleotide sequence which is at least 60% identical to a nucleic acid selected from the group consisting of a nucleic acid comprising nucleotides 1-528 of SEQ ID NO:3 or complement thereof and a nucleic acid comprising nucleotides 1-654 of SEQ ID NO:5.

123. An isolated nucleic acid selected from the group consisting of (a) a nucleic acid comprising a nucleotide sequence set forth in SEQ ID NO:3 or complement thereof and (b) a nucleic acid comprising a nucleotide sequence set forth in SEQ ID NO:5.

124. An isolated nucleic acid comprising a contiguous span of at least 17 nucleotides of the nucleic acid of claim 123.

125. The isolated nucleic acid of claim 124 comprising at least 21 nucleotides.

126. The isolated nucleic acid of claim 124 comprising at least 25 nucleotides.

127. The isolated nucleic acid of claim 124 comprising at least 30 nucleotides.

128. The isolated nucleic acid of claim 124 comprising at least 50 nucleotides.

129. An isolated nucleic acid comprising at least 21 nucleotides that encodes a contiguous span of at least 7 amino acids of a protein selected from the group consisting of a protein comprising an amino acid sequence set forth in SEQ ID NO:4 and a protein comprising an amino acid sequence set forth in SEQ ID NO:6.

130. The isolated nucleic acid of claim 129 encoding at least 8 contiguous amino acids.

131. The isolated nucleic acid of claim 129 encoding at least 9 contiguous amino acids.

132. The isolated nucleic acid of claim 129 encoding at least 10 contiguous amino acids.

133. The isolated nucleic acid of claim 129 encoding at least 15 contiguous amino acids.
134. The isolated nucleic acid of claim 129 encoding at least 20 contiguous amino acids.
- 5 135. The isolated nucleic acid of claim 129 encoding at least 25 contiguous amino acids.
136. A nucleic acid vector comprising the isolated nucleic acid of claim 117.
137. A nucleic acid vector comprising the isolated nucleic acid of claim 118.
- 10 138. A nucleic acid vector comprising the isolated nucleic acid of claim 119.
139. A nucleic acid vector comprising the isolated nucleic acid of claim 126.
- 15 140. A nucleic acid vector comprising the isolated nucleic acid of claim 132.
141. A host cell comprising the isolated nucleic acid of claim 117.
142. A host cell comprising the isolated nucleic acid of claim 118.
- 20 143. A host cell comprising the isolated nucleic acid of claim 119.
144. A host cell comprising the isolated nucleic acid of claim 116.
- 25 145. A host cell comprising the isolated nucleic acid of claim 132.
146. A microarray comprising the isolated nucleic acid of claim 132.
- 30 147. An isolated polypeptide selected from the group consisting of a polypeptide comprising an amino acid sequence set forth in SEQ ID NO:4 and a polypeptide comprising an amino acid sequence set forth in SEQ ID NO:6.

148. An isolated polypeptide selected from the group consisting of (a) a polypeptide comprising an amino acid sequence that is at least 70% identical to the amino acid sequence set forth in SEQ ID NO:4 and capable of interacting with ER-alpha and (b) a polypeptide comprising an amino acid sequence that is at least 70% identical to the amino acid sequence set forth in SEQ ID NO:6 and capable of interacting with ER-beta.

149. The isolated polypeptide of claim 148, wherein said ligand is ER-alpha.

150. The isolated polypeptide of claim 148, wherein said ligand is ER-beta.

151. An isolated polypeptide comprising a contiguous span of at least 8 amino acids of the polypeptide of claim 147.

152. The isolated polypeptide of claim 151 comprising a contiguous span of at least 10 amino acids.

153. The isolated polypeptide of claim 151 comprising a contiguous span of at least 12 amino acids.

154. The isolated polypeptide of claim 151 comprising a contiguous span of at least 15 amino acids.

155. The isolated polypeptide of claim 151 comprising a contiguous span of at least 17 amino acids.

156. The isolated polypeptide of claim 151 comprising a contiguous span of at least 20 amino acids.

157. The isolated polypeptide of claim 156 capable of interacting with a ligand selected from the group consisting of ER-alpha and ER-beta.

158. The isolated polypeptide of claim 157, wherein said ligand is ER-alpha.

159. The isolated polypeptide of claim 157, wherein said ligand is ER-beta.

5 160. An isolated polypeptide selected from the group consisting of (a) a polypeptide comprising an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of the amino acid sequence set forth in SEQ ID NO:4 of the same length, wherein said isolated polypeptide is capable of interacting with ER-alpha and (b) a polypeptide comprising an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of the amino acid sequence set forth in SEQ ID NO:6 of the same length, wherein said isolated polypeptide is capable of interacting with ER-beta.

161. The isolated polypeptide of claim 160, wherein said ligand is ER-alpha.

15 162. The isolated polypeptide of claim 160, wherein said ligand is ER-beta.

163. The isolated polypeptide of claim 160, wherein said amino acid sequence comprises from 8 to 20 amino acids.

20 164. The isolated polypeptide of claim 161, wherein said amino acid sequence comprises from 8 to 20 amino acids.

165. The isolated polypeptide of claim 162, wherein said amino acid sequence comprises from 8 to 20 amino acids.

25 166. An antibody which is specifically immunoreactive with the isolated polypeptide of claim 147.

30 167. An antibody which is specifically immunoreactive with the isolated polypeptide of claim 151.

168. A protein microarray comprising the isolated polypeptide of claim 147.

169. A protein microarray comprising the isolated polypeptide of claim 151.

170. A protein microarray comprising the isolated polypeptide of claim 163.

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171. A method for making an isolated polypeptide selected from the group consisting of a polypeptide comprising an amino acid sequence set forth in SEQ ID NO:4 and a polypeptide comprising an amino acid sequence set forth in SEQ ID NO:6, comprising:

providing an expression vector comprising a nucleic acid encoding said amino acid

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sequence; and

introducing said expression vector into a host cell such that said host cell producing the isolated polypeptide.

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